

REMARKS

Claims 8-12, 18, 21, 22, 26, 27, and 30-38 are pending and were rejected by the Examiner. In light of the following remarks and the attached declaration, Applicant respectfully requests allowance of all pending claims.

Rejections under 35 U.S.C. § 103

The Examiner rejected claims 8-12, 18, 21, 22 and 26 under 35 U.S.C. § 103(a) as being unpatentable over Tovey *et al.* in view of Brittenden *et al.* The Examiner stated that the Tovey *et al.* patent teaches treating various cancers with alpha-interferon doses ranging from 5000 U to 20×10^6 U, and preferably ranging from 1×10^4 U to 1×10^6 U. The Examiner further stated that the dosages recited in the Tovey *et al.* patent, when converted to the units used in the instant application, range from about 475,000 U/man to about 950,000 U/man. In addition, the Examiner stated that while the Tovey *et al.* patent fails to teach a method that includes determining NK cell cytotoxicity, the Brittenden *et al.* reference teaches that alpha-interferon enhances NK cell activity, and that NK cell activity plays an important role in natural cytotoxicity of cancer cells. Thus, the Examiner alleged that it would have been *prima facie* obvious to one of ordinary skill in the art to add steps of measuring NK cell cytotoxicity to the methods disclosed in the Tovey *et al.* patent.

The Examiner also rejected claims 27 and 30-38 under 35 U.S.C. § 103(a) as being unpatentable over Markovic *et al.* in view of Tovey *et al.* The Examiner stated that the Markovic *et al.* reference teaches that alpha-interferon acts to increase NK lymphocyte cytotoxicity, and that increased NK cytotoxicity is desired in the surgical treatment of cancer. The Examiner further stated that the Markovic *et al.* reference teaches a method for surgical removal of tumors from mice treated with alpha-interferon prior to surgery. In addition, the Examiner stated that while the Markovic *et al.* reference fails to teach methods for treating humans, the Tovey *et al.* patent teaches dosages of alpha-interferon that encompass the instantly claimed range of dosages. Thus, the Examiner alleged that it would have been *prima facie*

obvious to one of skill in the art to combine the teachings of the Markovic *et al.* reference with the teachings of the Tovey *et al.* patent to devise a method for treating humans.

Applicant respectfully disagrees with these rejections. Applicant also disagrees with the dosage calculations provided by the Examiner with regard to the Tovey *et al.* patent. The dosages disclosed in Tovey *et al.* patent range from 1500 U/man to 20×10^6 U/man for a 70 kg man. These values convert to a range of 806 U/m² to 10,752,688 U/m² if, as stated by the Examiner, the average 70 kg man has a surface area of about 1.86 m². This range is extremely broad. Even the "preferred" range of Tovey *et al.*, from 5376 U/m² to 537,634 U/m², covers a 100-fold difference in potential dosages. The instant claims, in contrast, recite dosages ranging from about 250,000 U/m² to about 500,000 U/m², a relatively narrow range that encompasses only a 2-fold difference in potential dosages. In view of the broad range taught by the Tovey *et al.* patent, the claimed range is surprisingly narrow. Moreover, the Tovey *et al.* patent does not teach or suggest that the effective dose within the disclosed broad range falls within the narrow range recited in the present claims.

Furthermore, the MPEP states that "Applicants can rebut a *prima facie* case of obviousness based on overlapping ranges by showing the criticality of the claimed range." MPEP § 2144.05. Enclosed herewith is a declaration under 37 C.F.R. § 1.132 signed by the Applicant. In the declaration, Applicant attests, *inter alia*, that the claimed range is critical for the clinical success of the claimed methods, and that the criticality of the claimed range could not have been predicted based on the teachings of the Tovey *et al.* patent.

Thus, Applicant submits that the claimed methods are not obvious over the cited references. Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 103.

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CONCLUSION

Applicant respectfully requests that claims 8-12, 18, 21, 22, 26, 27, and 30-38 be allowed. The Examiner is invited to telephone the undersigned if such would further prosecution. Applicant believes that no fees are due at this time. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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